Answer 1:

Bibliographic Information

Clonogenic assay with established human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. Fiebig, H. H.; Maier, A.; Burger, A. M. Oncotest GmbH, Institute for Experimental Oncology, Freiburg, Germany. European Journal of Cancer (2004), 40(6), 802-820. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:342988 AN 2004:284718 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pluripotent cells can be grown in clonogenic assays. The tumor stem-cell fraction, which accounts for <0.4% of the total cells, and which is considered the most relevant cell type in the development of metastases and recurrences, is able to divide and to form colonies in a semisolid matrix (agar or methylcellulose). Major applications of the tumor clonogenic assay (TCA) are chemosensitivity testing of tumors and xenografts, and for assessments within drug discovery programs. Of crit. relevance for the usefulness of the TCA is whether it can predict sensitivity or resistance towards clin. used agents. When we compared the response of human tumors established as xenografts in nude mice in the TCA in vitro to that of the clin. response, 62% of the comparisons for drug sensitivity, and 92% of the comparisons for drug resistance were correct. The same percentage of true/false observations was found when tumors were tested after serial passage in nude mice in the TCA in vitro and their response compared to in vivo activity in corresponding xenografts (60% and 90%, resp.). The highest correct predictive values were, however, found when the clin. response of tumors was compared to their explants established in the nude mouse and treated in vivo. Of 80 comparisons performed, we obsd. a correct prediction for tumor resistance in 97% and for tumor sensitivity in 90%. In our opinion, the TCA with established human tumor xenografts has an important role in current drug discovery strategies. We therefore included the TCA as secondary assay in our approach to anticancer drug discovery and found that a no. of novel agents were active; these are now in advanced preclin. development or clin. trials. Thus, the tumor clonogenic assay has proven predictive value in the chemosensitivity testing of std. and exptl. anticancer drugs.

Answer 2:

Bibliographic Information

Effect of a novel somatostatin analogue combined with cytotoxic drugs on human tumor xenografts and metastasis of B16 melanoma. Szende, B.; Horvath, A.; Boekoenyi, G.; Keri, G. 1st Dept. of Pathology and Experimental Cancer Res., Semmelweis Univ., Budapest, Hung. British Journal of Cancer (2003), 88(1), 132-136. Publisher: Nature Publishing Group, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 139:271238 AN 2003:71031 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A novel somatostatin analog, TT-232 (which inhibits the proliferation of various cell cultures and transplantable mouse tumors), was examd. regarding its effect on human melanoma and lymphoma xenografts as a single treatment or in combination with DTIC (dacarbazine) and etoposide. TT-232 inhibited the growth of HT-18 melanoma xenografts, a dose of 5 mg kg-1 being the most effective. Combination of 1 mg kg-1 TT-232 with 30 or 60 mg kg-1 DTIC (administered daily) resulted in a stronger inhibitory effect compared to TT-232 or DTIC as a single modality. Antimetastatic effect of TT-232 treatment combined with DTIC was studied using the B16 mouse melanoma muscle-lung metastasis model. The no. of lung metastases of B16 melanoma could be decreased by the daily administration of 1 mg kg-1 TT-232 or 60 mg kg-1, but not of 30 mg kg-1 DTIC. TT-232, combined with 30 or 60 mg kg-1 DTIC decreased the lung metastasis no. significantly lower than the control. Nearly 50% growth inhibition of HT-58 lymphoma was achieved by daily treatment with 1 mg kg-1 TT-232. 5 mg kg-1 etoposide, administered daily, resulted in a similar effect. The combination of 1 mg kg-1 TT-232 and 5 mg kg-1 etoposide was significantly more effective than TT-232 or etoposide as a single treatment. The very strong tumor growth inhibitory effect of 10 mg kg-1 etoposide could even be increased by combination with TT-232. These exptl. data suggest that TT-232 may be an effective new tool in the combination chemotherapy of malignant tumors like melanoma and lymphoma.

Answer 3:

Bibliographic Information

Combining radioimmunotherapy and chemotherapy for treatment of medullary thyroid carcinoma: Effectiveness of dacarbazine. Stein, Rhona; Chen, Susan; Reed, Linda; Richel, Heidi; Goldenberg, David M. Garden State Cancer Center, Belleville, NJ, USA. Cancer (New York, NY, United States) (2002), 94(1), 51-61. Publisher: John Wiley & Sons, Inc., CODEN: CANCAR ISSN: 0008-543X. Journal written in English. CAN 136:259269 AN 2002:57632 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background. To enhance the efficacy of chemotherapy for medullary thyroid carcinoma (MTC), we evaluated the effect of combining radioimmunotherapy (RAIT) with 90Y-anticarcinoembryonic antigen (CEA) monoclonal antibody MN-14 and chemotherapy in nude mice bearing human MTC xenografts. A preliminary study evaluated doxorubicin, dacarbazine (DTIC), cyclophosphamide, and vincristine, singly and in combination, for their effect on the growth of MTC xenografts (TT) in nude mice. Given individually, DTIC yielded the most effective tumor growth inhibition, delaying the mean time to doubling from 1 wk for untreated tumor-bearing mice to 7.5 wk. Administering either the 4 drugs in combination or a 2-drug combination comprised of doxorubicin and DTIC significantly improved the efficacy compared with any single drug alone, increasing the mean doubling time to 10-12 wk. Methods. Drug doses were selected to conform to the doses of each drug given clin. For the combined modality therapy, administration of 90Y-labeled anti-CEA monoclonal antibody MN-14 to nude mice bearing established TT tumors was followed by various chemotherapy regimens initiated 24 h after RAIT. Chemotherapy protocols combined with RAIT included doxorubicin or DTIC alone and in combination, and the doxorubicin, DTIC, cyclophosphamide, and vincristine 4-drug protocol. Tumor vols. were measured weekly, and toxicity was evaluated by measuring blood counts and body wt. Results. Combinations of RAIT and chemotherapy with DTIC or RAIT and chemotherapy with the drug combinations were found to augment the antitumor effects of RAIT or chemotherapy alone, without a significant increase in toxicity. The mean tumor vol. doubling times were increased up to 100% compared with the results of chemotherapy alone. No significant differences in tumor growth were obsd. between the RAIT plus DTIC protocol and the RAIT plus two- or four-drug protocols. Conclusions.

The superiority of the combined modality treatment argues for the integration of RAIT into chemotherapeutic regimens for MTC treatment. Clin. trials are needed to assess these principles in MTC patients.

Answer 4:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 5:

Bibliographic Information

The effect of tirapazamine (SR-4233) alone or combined with chemotherapeutic agents on xenografted human tumors. Lartigau, E.; Guichard, M. Laboratoire de Radiobiologie, Institut Gustave Roussy, Villejuif, Fr. British Journal of Cancer (1996), 73(12), 1480-1485. Publisher: Stockton, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 125:157937 AN 1996:471337 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Recent data have shown that the in vitro and in vivo cytotoxicity of bioreductive drugs could be significantly increased when combined with chemotherapy drugs such as cisplatinum, depending on the timing of administration. The aim of this study was to define the toxicity (animal lethality) and the activity (growth delay assay, excision assay) of a bioreductive drug, tirapazamine, alone and combined with chemotherapy agents (5-FU, VP16, bleomycin dacarbazine (DTIC) and cisplatinum) on nude mice bearing xenografted human tumors: a rectal carcinoma (HRT18) and a melanoma (Na11+). Animal lethality was markedly increased when tirapazamine at the LD 10% was combined with the other drugs. For the HRT18 tumor, the combination of tirapazamine and bleomycin significantly increased the delay of regrowth compared with bleomycin alone and was more cytotoxic than tirapazamine alone. For the Na11 + tumors the combination of tirapazamine with VP16 significantly increased tumor doubling time compared with the controls or VP16 alone. The combination of tirapazamine and VP16 was more cytotoxic than VP16 alone. When compared with cisplatinum or tirapazamine alone, there was a significant decrease in plating efficiency when tirapazamine and cisplatinum were given at the same time, but not when tirapazamine was given 3 h before cisplatinum. In conclusion, tirapazamine was shown to be cytotoxic against clonogenic human tumor cells. Its efficacy in vivo may depend on its combination with already active chemotherapy drugs on the tumor model used. The timing of administration may be less important than previously thought.

Answer 6:

Bibliographic Information

Predictability of clinical response to anticancer agents in human cancer xenografts. Tsukamoto, Fumine. Med. Sch., Osaka Univ., Suita, Japan. Osaka Daigaku Igaku Zasshi (1994), 46(4), 251-61. CODEN: ODIZAK ISSN: 0369-710X. Journal written in Japanese. CAN 121:124753 AN 1994:524753 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mouse transplanted human tumors retained original sensitivity to antitumor drugs, and was useful in secondary screening for the sensitivity to tumor chemotherapy. Fresh tumor tissues were transplanted and maintained in nude mice in 77 cases (tried: 247 cases), and sensitivity of the transplanted tumors to chemotherapy was compared between human therapy and in nude mice using regimen used clin. in 17 cases with 21 expts. (stomach, breast, colon, pancreas, esophagus. melanoma). Tested drugs were adriamycin, cisplatin, cyclophosphamide, cytarabine, dacarbazine, doxifluoridine, epirubicin, 5-fluorouracil, M-83 (a mitomycin C deriv.), mitomycin C, tegafur, and UFT. Chemotherapy in nude mice was effective in 6 expts., which coincided with clin. results in 5 cases. The ineffective 15 cases in nude mice coincided with the clin. results in all cases.

Answer 7:

Bibliographic Information

Effect of temozolomide and dacarbazine on O6-alkylguanine-DNA alkyltransferase activity and sensitivity of human tumor cells and xenografts to 1,3-bis(2-chloroethyl)-1-nitrosourea. Mitchell, R. Brian; Dolan, M. Eileen. Dep. Med., Univ. Chicago, Chicago, IL, USA. Cancer Chemotherapy and Pharmacology (1993), 32(1), 59-63. CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 119:173700 AN 1993:573700 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors investigated the ability of 5-(dimethyltriazeno)imidazole-4-carboxamide (DTIC, dacarbazine) and an analog, temozolomide, to deplete cells or tumors of O6-alkylguanine-DNA alkyltransferase (AGT) and to enhance the antitumor effects of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU). Human colon cancer (HT29) cell survival was decreased by almost 1 log when treated with 500 μM temozolomide prior to 150 μM BCNU. Administration of the maximal tolerated dose of DTIC (300 mg/kg) to nude mice carrying HT29 xenografts resulted in complete depletion of AGT activity in tumors at 4 h and 16 h. Administration of 150 mg/kg DTIC caused a 76% redn. in AGT activity at 4 h, but only a 28% redn. at 16 h. The maximally tolerated doses of DTIC and BCNU, alone and in combination, were used to treat nude mice bearing HT29 xenografts. No difference in tumor growth occurred when animals were treated with either BCNU alone (50 mg/kg), DTIC alone (300 mg/kg), DTIC (150 mg/kg) followed by BCNU (12.5 mg/kg), or BCNU (25 mg/kg) followed by DTIC (150 mg/kg). These data suggest that methylating agents such as DTIC may be too toxic to be used in combination with BCNU to deplete tumor alkyltransferase levels effectively and increase the therapeutic index of BCNU.

Answer 8:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 9:

Bibliographic Information

Childhood rhabdomyosarcoma xenografts: responses to DNA-interacting agents and agents used in current clinical therapy. Houghton, Janet A.; Cook, Ruby L.; Lutz, Pamela J.; Houghton, Peter J. Div. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, USA. European Journal of Cancer & Clinical Oncology (1984), 20(7), 955-60. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 101:163109 AN 1984:563109 CAPLUS

Abstract

A lab. model of childhood rhabdomyosarcoma (RMS) has been used to evaluate cytotoxic agents used in current clin. protocols, and DNA-reacting agents that have had either limited or no evaluation in this histiotype. Seven lines of RMS each derived from a different patient were grown as xenografts in immune-deprived mice, six of these being from specimens derived from previously untreated patients. Of the conventional' agents, vincristine [57-22-7] was the most effective. Of the other agents evaluated [L-phenylalanine mustard (L-PAM) [148-82-3], cis-dichlorodiammineplatinum (cis-DDP) [15663-27-1], mitomycin C [50-07-7] and

5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) [4342-03-4]], L-PAM caused complete regressions in six of seven lines, including those resistant to cyclophosphamide [50-18-0]. DTIC had marked activity in five tumors, and mitomycin C in three lines. Cyclophosphamide was active in five tumors, although efficacy was less marked in two lines in comparison to DTIC and mitomycin C.

Answer 10:

Bibliographic Information

Evaluation of the response of a panel of human melanoma tissue-cultured cell lines xenografted in nude mice to four anticancer drugs of known clinical activity. Bellet, Robert E.; Danna, Victoria; Mastrangelo, Michael J.; Eaton, Gordon J.; Berd, David. Fox Chase Cancer Cent., Philadelphia, PA, USA. Proceedings of the International Workshop on Nude Mice (1982), Volume Date 1979, 3rd(Vol. 2), 649-56. CODEN: PIWMDW ISSN: 0171-1784. Journal written in English. CAN 98:100654 AN 1983:100654 CAPLUS

Abstract

An evaluation of the predictability of a nude mouse-human melanoma panel as a secondary screen for cancer chemotherapeutic agents was undertaken. A total of 9 established human melanoma tissue-cultured cell lines heterografted in outbred Swiss nude mice was exposed to each of 4 single chemotherapeutic agents of known clin. activity against human melanoma (DTIC, BCNU = active; adriamycin, 5-azacytidine = inactive). For every cell line assay, each of 30 nude mice received a s.c. inoculation of 4 × 106 viable tumor cells. Upon tumifaction in all animals, 6 control mice received a single (i.p.) injection of sterile saline; simultaneously, 6 mice for each of the 4 test drugs received a single i.p. injection of only that drug administered at the predetd. LD10. Tumor sizes were measured weekly; each expt. was terminated 28 days post-treatment. At each measurement time point, control tumor vols. were compared with treated tumor vols. utilizing Student's t test. Statistically significant differences in tumor vol. in favor of drug-treated mice indicated chemotherapeutic response. Of the 9 cell lines exposed to the 4 chemotherapeutic agents, 4 lines were sensitive to DTIC; 3 were sensitive to BCNU; none of the lines was sensitive to adriamycin or 5-azacytidine. Thus, the nude mouse-human melanoma system may be sufficiently predictive to allow for the screening of chemotherapeutic agents of unknown clin. activity.

Answer 11:

Bibliographic Information

In vitro sensitivity of human melanoma xenografts to cytotoxic drugs. Correlation with in vivo chemosensitivity. Tveit, Kjell Magne; Fodstad, Oeystein; Olsnes, Sjur; Pihl, Alexander. Norwegian Cancer Society, Norsk Hydro's Inst. Cancer Res., Oslo, Norway. International Journal of Cancer (1980), 26(6), 717-22. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 94:76807 AN 1981:76807 CAPLUS

Abstract

Single-cell suspensions prepd. from 5 human melanomas, grown serially as xenografts in athymic nude mice, were exposed in vitro to increasing concns. of dacarbazine [4342-03-4], CCNU [13010-47-4], procarbazine [671-16-9], vinblastine [865-21-4], and the cancerostatic lectins abrin and ricin. The in vitro chemosensitivity of the cells, as measured by the drug concns. required to inhibit colony formation in soft agar by 50%, was correlated with the growth delay of the xenografts in vivo, previously obsd. after treatment of the animals with maximal tolerable doses of the same drugs. For each drug, the in vitro sensitivity of the different xenografts was strongly correlated with their response in vivo. Apparently, the soft agar test, as carried out here, adequately reflects the relative sensitivity of the xenografts in vivo. The data indicate that human xenografts may be used to develop quant. in vitro chemosensitivity tests.